THE UNIVERSITY OF WISCONSIN
COLLEGE OF AGRICULTURE

Madison 6

DEPARTMENT OF GENETICS

February 3, 1949.

Dear Art,

Thanks for your flattering letter: I haven't blushed so in years. You can be sure of being on my mailing list; the reprints of that Heredity just haven't come yet- right now they'r "passing through customs".

I saw your paper on B_2 and its photodynamic action. We're too tied up right now to embark on any mutagenic work, but didn't Burkholder do something along these lines at Yale? I recall that he used proflavine in this way, and got results which were interesting but not conclusive, and I seem th remember that at least he planned to try B_2 also. Can you not get similar effects with other fluorescent compounds? Does FAD have the same properties as free B_2?

Lately, I've been busy with two problems, both of which are probably going to be long-drawn-out affairs. The first is, of course, the gene enzyme story. It turns out that at least two out of the seven Lac- mutations are really capable of producing the galactosidase under special conditions. Lac_1- develops no activity in the presence of lactose, but when grown on galactose or butyl galactoside, adapts quite readily, and produces the enzyme. This leads to the paradox that lactose-grown cells have no activity on lactose, but cells grown on butyl galactoside, or less so on galactose, ferment lactose at a rapid rate! Clearly, the Lac_1- mutation has not affected the specificity of any enzyme, but altered

the conditions of its formation. Substrates which are not utilized (i.e. galactose in a Gal- mutant; lactobionate on wild type) can evoke the enzyme so it seems unlikely to me that the first step in enzyme adaptation is a combination of substrate with preformed enzyme. While writing, it occurs to me that there is not a yes-pr-no answer to the 1:1 theory. For adaptive enzymes, a rather complicated mechanism has been evolved which improves the flexibity of the cell; here there may weal be more indirect and more numerous relationships between gene and enzyme, than there are for the somewhat less variable enzymes involved in biosyntheses. Also, it may be that the probably smaller amounts needed of the biosynthetic ensymes/cell permit of a more direct relationship, in a physical way, between the gene and the enzyme. But I want to clean up the adaptive enzyme story (by 1960 or so) before tackling the constitutive enzymes. Meanwhile, the enzyme has been gotten out, sometimes partially purified, and a lot of kinetic work done on it (especially on an artefactual stimulation by Na) mostly for background, but also as a basis for comparative studies on the enzymes produced by various genotypes.

This work would be a lot further along if I hadn't accidentally found some heterozygous diploids coming out of some K-12 crosses, last summer. One of my stocks picked up a "mutation" somewhere which modifies the life cycle so that the diploid zygote does not always undergo immediate meiosis, but can be recovered and maintained as such. These lines are very unstable, and show some peculiarities that haven't been explained yet, but already have revolutionized what we can do in genetic analysis (F-2's, etc.)

We heard about your family, and sometimes wish we could be as far along. Esther is very very busy working on her degree, and has some very interesting stuff on genetic control of mutability in Lac- K-12.

Of course, I'm very glad to hear about any prospects of coming out to "Sunny California", especially with our -10^{0} weather here. I tried to plan to go west this summer, but was too late to swing it. We've just bought a car (just a '35 Chev) but it wouldn't do to travel in. If those prospects materialize, I just want to say that the Fall semester would be somewhat inconvenient, as I'll be teaching a course on microbial genetics that we're starting here. But any time before or after would be very joyfully considered.

Best regards from Esther, and to Dale,

Simcerely

Joshua